REMARKS

Claim 18 has been amended to specify that the monoclonal antibody is isolated/purified, and to remove the reference to the specific antigen used to generate the antibody. Claim 19 has been amended to be dependent upon claim 18 and to remove the reference to the specific antigen used to generate the antibody. Claims 20 and 21 have been amended to incorporate the limitation removed from claims 18 and 19. Claim 22 has been amended to place the claim in independent form. Claim 23 is amended to substitute "providing" for "synthesizing."

Claims 18-19 stand rejected under 35 USC § 102(b) as being anticipated by, or in the alternative, rejected under 35 USC § 103(a) as obvious over Hinds et al. (Journal of Medicinal Chemistry, 1991 vol. 34 pages 1777-1789). Applicants respectfully traverse.

First of applicants note that the claims specify that the claimed isolated monoclonal antibodies of the present invention have a binding affinity of greater than 10^8M^{-1}. The two monoclonal antibodies (DB19/1 and DB19/25) isolated by Hinds et al. are reported as having dissociation constants of 1.8×10^{-7} and 1.8×10^{-8} (see Table IV on page 1784 of that reference). Accordingly, the dissociation constants of the Hinds antibodies have binding affinities (the reciprocal of the dissociation constant) of 5.5×10^{-6} and 1.8×10^{-7}, respectively. Therefore, Hinds fails to teach an isolated monoclonal antibody that binds to the amino acid sequence YPYDVPDYA (SEQ ID NO: 1) with a binding affinity greater than 10^8M^{-1}.

To anticipate a reference must disclose each of the elements of the claimed invention. Applicants respectfully submit the Hinds reference fails to teach an isolated antibody that has the required binding affinity. Accordingly, applicants request the withdrawal of the rejection based on 35 USC § 102(b).

Claims 18-21 and 23-25 stand rejected under 35 USC § 103(a) as being unpatentable over as obvious over Hinds et al. (Journal of Medicinal Chemistry, 1991 vol. 34 pages 1777-1789) in view of Kuby (Immunology, Second Edition, WH Freeman and Company, 1994, pages 160-164). Applicants respectfully traverse.

Regarding the rejection of the claims for obviousness, the Examiner has stated that for a given antigen, the Kd "usually" varies from 10^{-7} M to 10^{-11}. In support of that statement the Examiner has made reference to a general survey immunology textbook.

First of all, applicants note that the relevant limitation of applicants' claim is directed to binding affinity not binding dissociation. The Examiner has not provided any evidence regarding whether the range cited for dissociation constants can be extended to binding affinities of antibodies. In addition, applicants respectfully submit that one of ordinary skill appreciates that such generic statements provided in survey textbooks may be true when discussing the general characteristics of antibodies in the abstract. However, skilled practitioners know that the quality of antibodies generated for individual antigens is highly variable. Thus contrary to the Examiner's assertion, one of ordinary skill in the art would not anticipate that antibodies having an affinity ranging over four orders of magnitude (i.e. 10^{-7} M to 10^{-11}) will be generated for each antigen subjected to standard antibody production procedures.

Although the technique underlying hybridoma technology is well recognized, the results obtained by its use are clearly unpredictable. Hybridoma technology is an empirical art in which the routineer is unable to foresee what particular antibodies will be produced and which specific surface antigens will be recognized by them. **Only by actually carrying out the requisite steps can the nature of the monoclonal antibodies be determined and ascertained; no "expected"**

results can thus be said to be present (emphasis added). Ex parte Old, 229 USPQ 196 (BPAI 1985). Accordingly, as recognized by the USPTO Board of Patent Appeals and Interferences, the ability of producing the high affinity antibodies of the present invention could not have been expected, and therefore cannot be obvious, absent specific evidence showing they can be produced.

The Examiner concludes that antibodies, having the high affinities of the present invention, can be produced using the methods disclosed in Hinds, without any evidence to support such statements for this particular antigen. A reference to a generic discussion of antibody dissociation rates does not make applicants high affinity antibodies to the peptide YPYDVPDYA obvious, given the unpredictability of the art. It merely constitutes an invitation to experiment.

Furthermore, applicants respectfully submit that experimenters typically select an antibody producing hybridoma form the available pool of hybridomas based on which hybridoma produces an antibody providing the strongest positive signal. Accordingly, one of ordinary skill would have reason to believe that two isolated antibodies DB19/1 and DB19/25 were the best antibodies produced by the Hinds et al methods. While the possibility exists that the methods disclosed by Hinds could generate antibodies having the high affinities of applicants' claimed antibodies, such a possibility is mere speculation, particularly given the unpredictable nature of antibody production.

Applicants have used a procedure that has resulted in the actual production of antibodies having a binding affinity of 10^9-$10^{10}M^{-1}$. Applicants respectfully submit that the Hinds et al reference fails to suggest that antibodies having a higher affinity than those disclosed therein could be obtained, and fails to provide a sufficient teaching of how to obtain such high affinity

antibodies. Applicants respectfully submit that "obvious to try" is not the standard under 35 USC § 103, and that Hinds is merely an invitation to experiment.

Regarding claims 23-25, the Examiner notes that procedures for generating hybridomas and antibodies have been previously disclosed and that selection of a particular cell line and/or animal merely constitutes conventional substitutions of the components used in Kuby. However, applicants note that applicants have used a novel starting material (a 14 amino acid sequence, specifically disclosed in claim 24) to generate a novel product. Applicants respectfully submit that an otherwise old process, wherein a previously unknown starting material is used to make a novel final product, is patentable when the prior art fails to suggest the final product or the use of the specific starting material in the claimed process (see In re Ochiai, 71 F3d 1565, 37 USPQ2d 1127, 1131 (FED Cir 1995)). The cited references fail to provide any motivation for using an epitope consisting of 13 or 14 amino acids, or more particularly the specific amino acids disclosed in claim 24. Accordingly applicants respectfully request the withdrawal of the rejection of claims 18-21 and 23-25 under 35 USC § 103(a).

Applicants believe that the present application is now in condition for allowance and such action is respectfully requested. If the Examiner has any questions or comments such that a conversation would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,

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